REMARKS

The Examiner provides a number of rejections and we list them here in the order in which they are addressed:

I. Rejections Under 35 U.S.C. § 112

A. Claims 12-15 and 39 are rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

B. Claims 12, 14 and 15 are rejected as allegedly nonenabled.

C. Claims 12, 14, 15 and 39 are rejected for allegedly containing subject matter that is not described in the specification in such a way as to show possession.

II. Claims 12, 14 and 15 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yen *et al.*, Nature, 359:536-539 (1992).

III. Claim 39 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Brown *et al.*, J Cell Biol, 125:1303-12 (1994), in view of Hyman *et al.*, Nature, 351:206-211 (1991).

I. The Claims Are Not In Violation Of 35 U.S.C. § 112

A. Claims 12-15 and 39 Are Not Indefinite

The Examiner rejects Claim 12 because the percent identity language does not recite the intended amino acid sequence. The Applicants respectfully disagree. Claim 12 recites a CENP-E nucleic acid sequence encoding a protein that is fully disclosed within the specification. It is well settled patent law that the claims may be interpreted by the written description.

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claim 12 to specify the encoded protein has homology to a protein comprising SEQ ID NO:1.

The Examiner rejects Claims 12 and 39 as indefinite because they contain the abbreviation CENP-E. The Applicants respectfully disagree. The CENP-E abbreviation is

fully defined within the specification. It is well settled patent law that the claims may be interpreted by the written description.

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claim 12 that replaces the abbreviation CENP-E with the definition "centromere-associated protein E". *Applicants' Specification, pg. 20, ln 8.* The Applicants have elected to cancel claim 39, without prejudice, in order to further expedite the prosecution of the application.[1]

B. Claims 12, 14 and 15 Are Enabled

The Examiner allegedly rejects Claims 12, 14 and 15 in that they do not "... reasonably provide enablement for the full scope of nucleic acid sequences encoding proteins comprising core motor domains ... which proteins specifically bind to antibodies raised against CENP-E." *Office Action, pg 4, ¶ 4.* The Applicants respectfully disagree.

Applicants' specification provides sufficient teachings that are applicable to all related kinetochore proteins and their associated nucleic acids; the CENP-E protein is merely exemplary. One of skill in the art may easily adapt, without undue experimentation, the Applicants' example of CENP-E to a wide variety of kinetochores. Similarly, the production of epitope-specific antibodies, while empirical in nature, is also easily adapted by those skilled in the art from the specific teachings of the Applicants' specification.

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended independent Claim 12 to recite that the encoded amino acid sequence "comprises residues 1-324 of SEQ ID NO:1" and has "a plus end-directed microtubule motor domain", while simultaneously removing, without prejudice, the "antibody-binding" and the "plus-end directed activity" functional recitations. This amendment of Claim 12 resolves the rejection of Claim 15, since it is a dependent claim. Dependent Claim 14 is canceled, without prejudice, in order to further expedite the prosecution of the application.[2]

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[1] Claim 39 is cancelled to further business goals and not in acquiescence to a rejection. Indeed, the right to prosecute Claim 39 in the future is hereby expressly reserved.

[2] Claim 14 is cancelled to further business goals and not in acquiescence to a rejection. Indeed, the right to prosecute Claim 14 in the future is hereby expressly reserved.

C. Claims 12, 14, 15 and 39 Contain Described Subject Matter

The Examiner states that Claims 12, 14, 15 and 39 are rejected "... as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the invention was filed, had possession of the invention. *Office Action, pg 6 ¶ 5.* The Applicants disagree.

To support this rejection the Examiner relies on a Federal Circuit case holding explained in *University of California v. Eli Lilly and Co.,* 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). *Office Action, pg. 6 ¶ 5.* Specifically, the Examiner cites *Lilly* for:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus **or of a recitation of structural features common to the members of the genus**, which features constitute a substantial portion of the genus. *Office Action, pg. 6 ¶ 5* [emphasis added]

The Examiner concludes that the Applicants fail to provide a recitation of structural features common to members of the genus. The Applicants disagree.

The holding set forth in *Lilly* allows a genus claim when the specification discloses a common structural feature (see highlighted language quoted above). Applicants point out that the specification clearly teaches the "plus end-directed motor core protein" as a novel common structural feature:

> The present invention provides for the **first time** biologically active CENP-E and demonstrates that CENP-E has **a plus end-directed** microtubule motor activity. *Applicants' Specification, pg 8 ln 3-4.* [emphasis added]

and,

> The term "motor domain" or "core motor domain" refers to the domain of CENP-E that **confers the plus end-microtubule motor activity** on the protein. "CENP-E" refers to ... the **kinesin superfamily** of microtubule motor proteins. CENP-E is an **integral component** of the kinetochore structure of the chromosome, which links the chromosome to the spindle microtubules. *Applicants' Specification, pg 20 ln 6-11.* [emphasis added]

The Applicants refer the Examiner to the passages below that clearly indicate CENP-E plus-end directed motor proteins are required for mitosis in all species and is not intended to be

limited to *Xenopus*:

> Within the core of the motor domain (residues 1-324) XCENP-E and human CENP-E ('hCENP-E") share 74% identity (Moore et al., Bioessays 18:207-219 (1996). *Applicants' Specification, pg. 8 ln 24-26.*

and,

> CENP-E is a plus end-directed microtubule motor that is **required for mitosis**. The present invention provides for the first time biologically active CENP-E. *Applicants' Specification, pg 37, ln 28-29.* [emphasis added]

and,

> Because plus end-directed microtubule motor activity of CENP-E is **essential for mitosis**, inhibition of CENP-E can be used to control cell proliferation. *Applicants' Specification, pg. 38, ln 11-13.* [emphasis added]

and,

> These findings indicate that during normal mitotic spindle formation, **CENP-E plays an essential role** in mitotic spindle assembly and in prometaphase chromosome movements that result in metaphase chromosome alignment, **via its activity as a plus-end directed microtubule motor activity**. *Applicants' Specification, pg. 52 ln 26-29.* [emphasis added]

The above teachings show the Applicants' specification teaches that mitosis, in general, requires a plus-end directed CENP-E from any species, and therefore, is clearly not limited to *Xenopus* (*i.e.*, XCENP-E) as the Examiner has suggested. The Applicants provide above a detailed explanation that **all** centromere-associated proteins having plus end-directed activity (*i.e.*, CENP-E) share a common structural feature of the plus-end directed core motor domain.

Moreover, for other reasons (explained in the previous section), Applicants have amended Claim 12 to further clarify a plus end-directed microtubule motor domain that, in *Xenopus*, is encoded amino acid sequence comprising residues 1-324 of SEQ ID NO:1. thus, not only is a common structural feature described in the specification, but now Claim 12 describes this structural feature as a specific sequence that can be used as a reference point. Applicants, therefore, respectfully request the Examiner withdraw the rejection.

Importantly, the Examiner concedes that the specification is "enabling for nucleic acid sequences that encode the amino acid sequence of SEQ ID NO:1, or encode a protein comprising the amino acids sequence of 1-324 of SEQ ID NO:1 . . ." (Office Action, bottom

of page 3 to the top of page 4). New Claim 43, therefore, should not be subject to this rejection.

II. Claims 12, 14 and 15 Are Not Anticipated

The Examiner has rejected Claims 12, 14 and 15 as allegedly being anticipated under 35 U.S.C. § 102(b) by Yen *et al.*. In particular, the Examiner states "Yen [*et al.*] teaches a human CENP-E nucleic acid that encodes a protein which has greater than 70% identity to amino acids 1-324 of SEQ ID NO:1 ... [and] ... that the encoded protein has a molecular weight of 312 kDa." *Office Action, pg. 8 ¶ 6.* Applicants must respectfully disagree, as Applicants believe Yen *et al.* do not anticipate the presently amended preferred embodiment.

As the Examiner is well aware, a single reference must disclose each limitation of a claim in order for that reference to anticipate the claim. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). This criterion is not met with the Yen *et al.* reference.

The Applicants argue that the Examiner overlooks the fact that the present invention contemplates a variety of sequence identities to SEQ ID NO:1 encompassed within pending Claims 12, 14 and 15 by the use of the transition term "comprising". Specifically, the Examiner is requested to review the following exemplary paragraph:

> In one embodiment, the CENP-E protein has an amino acid sequence having at least 34%, or alternatively at least 45%, or alternatively at least 55% sequence identity with a XCENP-E motor domain of SEQ ID NO:1. Alternatively, CENP-E has at least 60%, 65%, or 70% sequence identity with a XCENP-E motor domain of SEQ ID NO:1. In an alternative embodiment, the CENP-E has 70%, or alternatively 75% or **alternatively 80%, or alternatively 85%**,or alternatively 90% or alternatively 95% amino acid sequence identity ... *Applicants' Specification, pg 4 ln 15 - 20.* [emphasis added]

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claim 12 to recite "... a protein having a plus-end directed core motor domain that has greater than 80% amino acid sequence identity to a *Xenopus* centromere-associated protein E core motor domain ....". Additionally, Applicants have added new Claims 44-46 to recite other embodiments supported by the above citation to the specification.

The Examiner admits that Yen *et al.* does not teach an amino acid sequence having greater than 80% amino acid sequence identity with amino acid residues 1-324 of SEQ ID NO:1. Thus, Applicants submit that both amended Claim 12 and Claim 15 are novel and respectfully request the Examiner withdraw the rejection.

III. Claim 39 Is Not Obvious

Applicants argue (without agreeing with the Examiner) this rejection is now moot, as a consequence of the cancellation of Claim 39 as explained *supra*. Applicants respectfully request the Examiner withdraw the rejection.

CONCLUSION

The Applicants believe that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.252.3353.

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